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Original Research Article

Operative Profile and Surgical Outcomes of COVID-19-Associated Mucormycosis: A Retrospective Observational Study

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Conflict of interest: Nil

Abstract:

Background: Coronavirus disease-2019 (COVID-19)-associated mucormycosis (CAM) emerged as a serious opportunistic fungal infection during the COVID-19 pandemic, particularly in patients with diabetes mellitus and corticosteroid exposure. Surgical debridement combined with antifungal therapy is the mainstay of treatment; however, predictors of surgical outcomes and mortality require further evaluation.

Aim and Objectives: To evaluate the operative profile, surgical outcomes, and predictors of mortality in patients with COVID-19-associated mucormycosis undergoing surgical management at a tertiary care center.

Materials and Methods: This retrospective observational study included 60 patients with confirmed COVID-19-associated mucormycosis who underwent surgical intervention between June 2021 and May 2022. Clinical, radiological, operative, and outcome data were retrieved from hospital medical records.

Results: The mean age of patients was 52.4 ± 11.6 years, with male predominance (68.3%). Diabetes mellitus was present in 86.7% of patients, and 81.7% had received corticosteroids during COVID-19 treatment. Sinonasal involvement was observed in 46.7%, rhino-orbital in 33.3%, and rhino-orbito-cerebral involvement in 20.0% of patients. Endoscopic sinus debridement was performed in all patients, while 23.3% required maxillectomy and 10.0% required orbital exenteration. At 90-day follow-up, 68.3% of patients recovered, 16.7% had residual disease, and overall mortality was 31.7%. Mortality was significantly higher in patients with intracranial involvement ($p = 0.0008$) and in those undergoing extensive surgical procedures ($p = 0.0003$).

Conclusion: COVID-19-associated mucormycosis is associated with high mortality, particularly in advanced disease. Early diagnosis, aggressive surgical debridement, and prompt antifungal therapy are essential for improving survival. Disease extent remains the most important predictor of outcome.

Keywords: COVID-19, Mucormycosis, Rhino-Orbito-Cerebral Mucormycosis, Surgical Outcomes, Orbital Exenteration, Mortality.

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Introduction

Mucormycosis is a rapidly progressive, angioinvasive fungal infection caused by fungi of the order Mucorales and primarily affects immunocompromised individuals, especially those with uncontrolled diabetes mellitus, diabetic ketoacidosis, malignancies, organ transplantation, and prolonged corticosteroid therapy [1]. The hallmark of the disease is vascular invasion leading to thrombosis, ischemia, and tissue necrosis, resulting in high morbidity and mortality if not treated promptly. Rhino-orbito-cerebral mucormycosis (ROCM) is the most frequent clinical form, typically beginning in the nasal mucosa and paranasal sinuses and potentially extending to the orbit and brain [2].

During the COVID-19 pandemic, a dramatic increase in mucormycosis cases was observed,

particularly in India, leading to the emergence of COVID-19-associated mucormycosis (CAM) as a major public health concern [3]. This surge has been attributed to immune dysregulation caused by SARS-CoV-2 infection, injudicious corticosteroid use, uncontrolled hyperglycemia, and prolonged hospitalization [4]. Corticosteroids impair neutrophil function and worsen glycemic control, thereby increasing susceptibility to invasive fungal infections [5]. Diabetes mellitus remains the most important predisposing factor, as hyperglycemia enhances fungal growth, impairs host immunity, and increases iron availability, facilitating fungal invasion [6].

Clinically, CAM commonly presents with nasal obstruction, facial pain, periorbital swelling, and headache, progressing to vision loss and intracranial complications in advanced stages [2,8]. Management requires early diagnosis, prompt antifungal therapy with liposomal amphotericin B, and aggressive surgical debridement to remove necrotic tissue and reduce fungal burden [1,9]. Surgical intervention plays a crucial role in improving survival but is associated with significant morbidity and perioperative challenges. Therefore, this retrospective observational study was conducted to evaluate the operative profile and surgical outcomes of CAM patients at a tertiary care center.

Materials and Methods

Study design and setting: This retrospective observational study was conducted in the Department of Otorhinolaryngology and Head and Neck Surgery in collaboration with the Departments of Ophthalmology, General Medicine, Anaesthesiology, Radiology, and Microbiology at a tertiary care teaching hospital in India. The study included patients treated between June 2021 and May 2022 during the peak surge of COVID-19-associated mucormycosis. Data were collected retrospectively from hospital records, operative notes, microbiology reports, and follow-up records.

Study Population: Hospital medical records were reviewed to identify eligible patients. All consecutive adult patients aged 18 years and above presenting with COVID-19-associated mucormycosis and undergoing surgical management at the study center during the study period were included. COVID-19 infection was confirmed by reverse transcriptase polymerase chain reaction (RT-PCR), rapid antigen test, or high-resolution computed tomography (HRCT) chest findings suggestive of COVID-19 within the preceding six weeks.

The diagnosis of mucormycosis was established based on clinical features, radiological findings, and microbiological or histopathological confirmation. Microbiological confirmation was obtained by potassium hydroxide (KOH) mount and fungal culture. At the same time, histopathological diagnosis was based on the demonstration of broad, aseptate, ribbon-like fungal hyphae with right-angle branching.

Patients with non-COVID mucormycosis, those who were medically unfit for surgery, patients managed conservatively without surgical intervention, and those with incomplete medical records were excluded from the study.

Clinical Evaluation: Clinical data at admission were retrieved from patient medical records. Demographic data, including age and gender, were recorded. Clinical history included duration and severity of COVID-19 illness, history of diabetes mellitus, corticosteroid use, oxygen therapy, intensive care unit admission, and other comorbidities.

A thorough otorhinolaryngological examination was performed, including diagnostic nasal endoscopy to assess the extent of disease and to obtain tissue samples for microbiological and histopathological examination. Ophthalmological and neurological examinations were performed in patients with suspected orbital or intracranial involvement.

Radiological assessment and disease classification: Radiological findings were obtained from imaging records including contrast-enhanced computed tomography (CECT) and/or magnetic resonance imaging (MRI) of the nose, paranasal sinuses, orbit, and brain to determine the extent of disease.

Based on clinical and radiological findings, patients were classified into three groups:

- Sinonasal mucormycosis
- Rhino-orbital mucormycosis
- Rhino-orbito-cerebral mucormycosis

This classification was used to assess disease severity and analyze outcomes.

Medical Management: All patients received systemic antifungal therapy in accordance with institutional protocol and international guidelines. Liposomal amphotericin B was administered intravenously at a dose of 5 mg/kg/day. The dose was adjusted based on renal function and patient tolerance. Renal function tests and serum electrolytes were monitored regularly during treatment.

After clinical stabilization and completion of initial therapy, patients were transitioned to oral posaconazole as step-down antifungal therapy.

Simultaneously, metabolic abnormalities such as hyperglycemia and electrolyte imbalance were corrected. Corticosteroids were discontinued or tapered whenever feasible.

Surgical Management: All patients underwent surgical intervention under general anesthesia. The type and extent of surgery were determined based on clinical and radiological findings.

The surgical procedures performed depended on the extent of disease involvement. These included endoscopic sinus debridement for removal of necrotic sinonasal tissue, medial maxillectomy in cases with maxillary involvement, and orbital decompression when the orbit was affected to preserve function. In advanced cases with extensive orbital necrosis, orbital exenteration was performed to achieve complete disease clearance and prevent further spread.

The primary objective of surgery was the complete removal of all necrotic and infected tissue until healthy bleeding margins were achieved.

Intraoperative parameters obtained from operative records included duration of surgery, estimated blood loss, extent of disease involvement, and type of surgical procedure performed. Patients were closely followed postoperatively, and revision surgery was undertaken in cases with residual or progressive disease detected during the follow-up period.

Outcome Measures: Follow-up data up to 90 days after discharge were obtained from follow-up records. Patient outcomes were categorized into three groups: recovery, defined as complete clinical and radiological resolution of disease; residual disease, indicating persistent infection requiring additional treatment; and death during the course of management or follow-up.

Statistical Analysis: Data were extracted from medical records and entered into Microsoft Excel and analyzed using the Statistical Package for the Social Sciences (SPSS) version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation, while categorical variables were expressed as frequency and percentage. Association between categorical variables was analyzed using the Chi-square test or Fisher's exact test as appropriate. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 60 patients with COVID-19-associated mucormycosis were included in this retrospective study. The mean age of the study population was 52.4 ± 11.6 years (range: 29–74 years), with the majority of patients belonging to the 51–60 years age group. Male patients accounted for the majority of the study population. A large proportion of patients had pre-existing diabetes mellitus, and most had received systemic corticosteroids and oxygen therapy during the management of COVID-19 illness, indicating the presence of established metabolic and treatment-related risk factors for mucormycosis in this cohort (Table 1).

Table 1: Demographic and Clinical Characteristics of the Study Population (n = 60)

Variable	Frequency	Percentage
Age <40 years	11	18.3
41–50 years	17	28.3
51–60 years	20	33.3
>60 years	12	20.0
Male	41	68.3
Female	19	31.7
Diabetes Mellitus	52	86.7
Steroid use	49	81.7
Oxygen therapy	38	63.3

Figure 1: Clinical photograph showing right-sided rhino-orbital mucormycosis

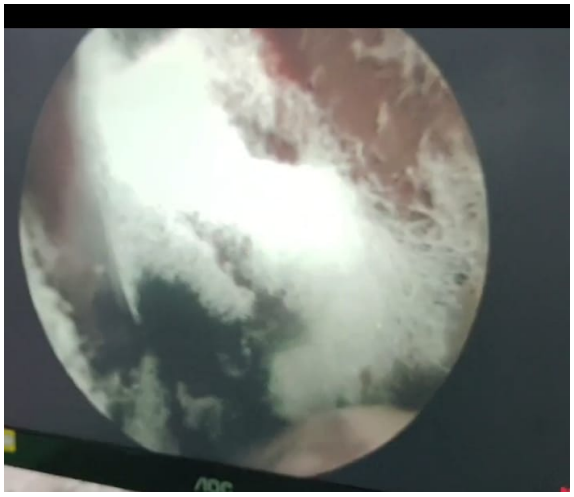

Figure 2: Endoscopic picture of extensive mucour in left nasal cavity and maxillary sinus

Based on clinical and radiological evaluation, patients were categorized according to the extent of disease involvement. Sinonasal mucormycosis was the most common presentation, followed by rhino-orbital disease, while intracranial extension was observed in a smaller but clinically significant proportion of patients. The distribution of disease extent is summarized in Table 2 and illustrated in Figure 3.

Table 2: Distribution of Disease Extent (n = 60)

Disease extent	Frequency	Percentage
Sinonasal	28	46.7
Rhino-orbital	20	33.3
Rhino-orbito-cerebral	12	20.0

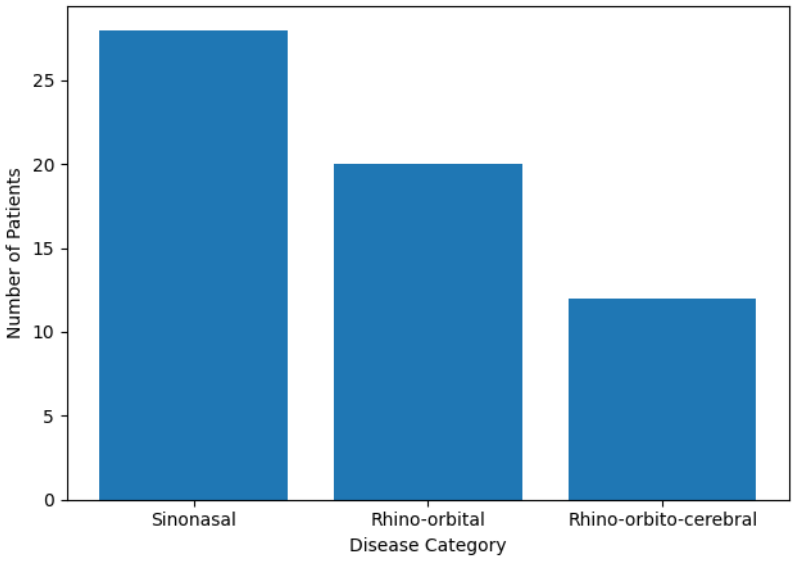

Figure 3: Distribution of Disease Extent in the Study Population. Bar diagram showing sinonasal, rhino-orbital, and rhino-orbito-cerebral involvement.

All patients underwent surgical intervention as part of a combined medical and surgical management plan. Endoscopic sinus debridement was performed in all cases, while additional extensive surgical procedures were required depending on the severity and extent of disease. These included maxillectomy, orbital decompression, and orbital exenteration. Revision surgery was required in a subset of patients due to persistent or progressive disease. The

distribution of surgical procedures performed is shown in Table 3.

Table 3: Surgical Procedures Performed (n = 60)

Surgical procedure	Frequency	Percentage
Endoscopic sinus debridement	60	100
Maxillectomy	14	23.3
Orbital decompression	8	13.3
Orbital exenteration	6	10.0
Revision surgery	11	18.3

At the 90-day follow-up, the majority of patients had complete recovery. In contrast, a proportion of patients had residual disease, and others succumbed to the illness, resulting in an overall mortality rate of 31.7%. The detailed outcome distribution is presented in Table 4 and depicted in Figure 4.

Table 4: Surgical Outcomes at 90 Days (n = 60)

Outcome	Frequency	Percentage
Recovery	41	68.3
Residual disease	10	16.7
Mortality	19	31.7

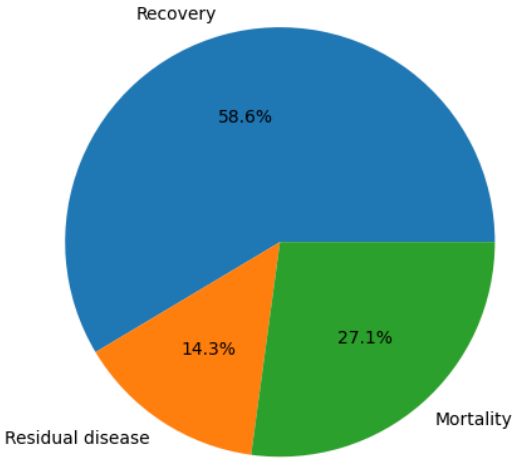

Figure 4: Overall Surgical Outcome at 90 Days. Pie chart showing recovery, residual disease, and mortality.

Further analysis demonstrated a significant association between disease extent and mortality. Mortality increased markedly with disease progression, with the highest mortality observed in patients with rhino-orbito-cerebral mucormycosis. This association was statistically significant (χ^2 = 14.34, df = 2, p = 0.0008), as shown in Table 5.

Table 5: Association Between Disease Extent and Mortality

Disease extent	Mortality (n)	Mortality (%)
Sinonasal	4	14.3
Rhino-orbital	6	30.0
Rhino-orbito-cerebral	9	75.0

Similarly, the type of surgical intervention was significantly associated with patient outcome. Patients undergoing extensive surgical procedures such as orbital exenteration demonstrated higher mortality compared to those undergoing endoscopic debridement alone. This association was statistically significant (χ^2 = 18.62, df = 3, p = 0.0003), as illustrated in Figure 5.

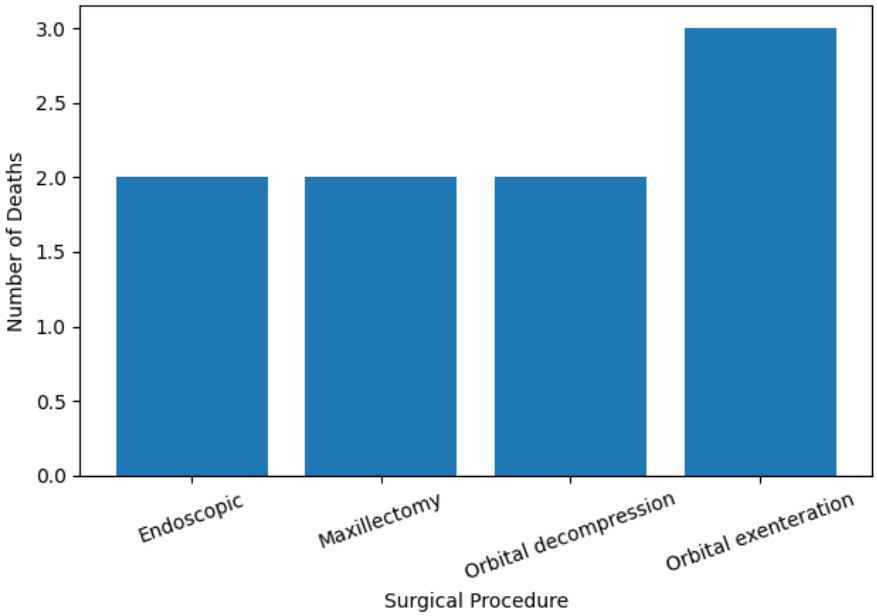

Figure 5: Mortality According to Type of Surgical Procedure. Bar diagram showing mortality rates for endoscopic debridement, maxillectomy, orbital decompression, and orbital exenteration.

In addition, prolonged operative duration was significantly associated with increased mortality. Patients undergoing surgery lasting more than 4 hours had significantly poorer outcomes than those with shorter operative duration ($\chi^2 = 11.42$, df = 2, p = 0.003).

Overall, these findings indicate that advanced disease stage and the need for extensive surgical intervention are major determinants of mortality in patients with COVID-19-associated mucormycosis.

Discussion

The present study demonstrated an overall mortality rate of 31.7%, with significantly higher mortality observed in patients with advanced disease, particularly those with intracranial involvement. These findings highlight the aggressive nature of CAM and the critical importance of early diagnosis and prompt surgical intervention.

In the present study, the majority of patients were middle-aged males, with a mean age of 52.4 years. This demographic profile is consistent with previous multicenter studies conducted in India during the COVID-19 pandemic. Patel et al. reported, in a large multicenter epidemiological study of 287 CAM patients, a median age of 52 years and male predominance, findings similar to ours [3]. The higher prevalence in males has been attributed to increased exposure to environmental pathogens and a higher prevalence of diabetes and other comorbidities in males.

Diabetes mellitus was the most common underlying comorbidity in the present study, observed in 86.7% of patients. This finding is consistent with multiple studies that have identified diabetes as the most important risk factor for CAM. Singh et al. reported diabetes in 80% of patients in a systematic review of 101 CAM cases [6]. Similarly, Moorthy et al. reported diabetes in 78% of CAM patients and emphasized that uncontrolled hyperglycemia impairs neutrophil chemotaxis and phagocytosis, thereby facilitating fungal invasion [5]. Hyperglycemia also increases the availability of free iron, which promotes fungal growth and angiogenesis [9].

Corticosteroid use was present in 81.7% of patients in the present study, highlighting its role as a major predisposing factor. Corticosteroids, although lifesaving in severe COVID-19, suppress immune function and worsen hyperglycemia, increasing susceptibility to opportunistic fungal infections. A systematic review by John et al. described the combination of diabetes, corticosteroid therapy, and COVID-19-induced immune dysfunction as a "perfect storm" for the development of mucormycosis [7].

The present study demonstrated that mortality increased significantly with disease extent, with the highest mortality observed in patients with rhino-orbito-cerebral mucormycosis. This finding is consistent with previous studies. Honavar reported mortality rates exceeding 50% in patients with intracranial involvement compared to less than 20% in patients with localized disease [2]. Similarly, Patel et al. reported that cerebral involvement was independently associated with increased mortality in CAM patients [3]. Intracranial spread indicates advanced angioinvasion and vascular thrombosis, both of which significantly reduce treatment success.

Surgical intervention plays a critical role in the management of mucormycosis. In the present study,

all patients underwent surgical debridement, and more extensive procedures such as maxillectomy and orbital exenteration were required in advanced disease. Mortality was significantly higher in patients undergoing orbital exenteration. This finding reflects disease severity rather than the surgical procedure itself. Sen et al. reported that orbital exenteration is often required in advanced disease and is associated with poor prognosis due to intracranial extension [4]. Surgical debridement improves survival by reducing fungal burden and enhancing antifungal drug penetration [1].

The overall mortality rate of 31.7% observed in the present study is comparable to previously reported mortality rates. A multicenter study by Patel et al. reported mortality of 28%, while Singh et al. reported mortality ranging from 25% to 49% depending on disease severity [2,6]. These findings confirm that despite aggressive medical and surgical management, CAM remains associated with high mortality.

Early diagnosis and prompt treatment are critical determinants of survival. Delayed surgical intervention allows disease progression and increases mortality. Cornely et al., in the global guideline for mucormycosis management, emphasized that early surgical debridement combined with liposomal amphotericin B significantly improves survival [1]. Similarly, Moorthy et al. demonstrated that delayed surgery was associated with poor outcomes [5].

The need for revision surgery in a subset of patients in the present study reflects the aggressive and invasive nature of mucormycosis. Complete surgical clearance is often challenging due to angioinvasion and tissue necrosis. Similar revision rates have been reported in previous studies [8].

The present study also highlights the importance of a multidisciplinary approach involving otorhinolaryngologists, ophthalmologists, physicians, anesthesiologists, and microbiologists. Early diagnosis, aggressive surgical management, strict glycemic control, and appropriate antifungal therapy are essential for improving outcomes.

Limitations

This was a single-center study with a relatively small sample size, which may limit the generalizability of the findings. Additionally, the follow-up period was limited to 90 days, and long-term outcomes and functional recovery could not be assessed. The retrospective design may introduce selection and information bias.

Conclusion

COVID-19-associated mucormycosis is an aggressive and life-threatening opportunistic infection with high morbidity and mortality. The present study highlights that early surgical intervention combined with appropriate antifungal therapy significantly improves survival. Advanced disease, especially with orbital and intracranial involvement and the requirement for extensive surgery, was associated with higher mortality. These findings underscore the importance of early diagnosis, prompt surgical debridement, strict glycemic control, and a multidisciplinary approach. Timely recognition and management remain essential to reduce mortality and prevent disease progression.

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